

FIGURE 1

A: BoNTA(H<sub>c</sub>) synthetic gene (Version #1) SEQ ID NO: 1

GAATTCGAAACGatgCGTCTGCTGTCTACCTTCACTGAATACATCAAGAAC  
ATCATCAATACCTCCATCCTGAACCTGCGCTACGAATCCAATCACCTGAT  
CGACCTGTCTCGCTACGCTTCCAAAATCAACATCGGTTCTAAAGTAACT  
TCGATCCGATCGACAAGAATCAGATCCAGCTGTTCAATCTGGAATCTTCC  
AAAATCGAAGTTATCCTGAAGAATGCTATCGTATACAACTCTATGTACG  
AAAATTCTCCACCTCCTTCTGGATCCGTATCCCGAAATACTTCAACTCC  
ATCTCTCTGAACAATGAATACACCATCATCAACTGCATGGAAAACAATT  
CTGGTTGGAAAGTATCTCTGAACCTACGGTGAAATCATCTGGACTCTGCAG  
GACACTCAGGAAATCAAACAGCGTGTGTATTCAAATACTCTCAGATGA  
TCAACATCTCTGACTACATCAATCGCTGGATCTTCGTTACCATCACCAAC  
AATCGTCTGAATAACTCCAAAATCTACATCAACGGCCGTCTGATCGACC  
AGAAACCGATCTCCAATCTGGGTAACATCCACGCTTCTAATAACATCATG  
CTTCAATCTGTTTCGACAAAGAAGTGAACGAAAAAGAAATCAAAGACCTG  
TACGACAACCAAGTCCAATTCTGGTATCCTGAAAGACTTCTGGGGTGACTA  
CCTGCAGTACGACAAACCGTACTACATGCTGAATCTGTACGATCCGAAC  
AAATACGTTGACGTCAACAATGTAGGTATCCGCGGTTACATGTACCTGA  
AAGGTCCGCGTGGTTCTGTTATGACTACCAACATCTACCTGAACTCTTCC  
CTGTACCGTGGTACCAAATTCATCATCAAGAAATACGCGTCTGGTAACA  
AGGACAATATCGTTCGCAACAATGATCGTGTATACATCAATGTTGTAGTT  
AAGAACAAGAATACCGTCTGGCTACCAATGCTTCTCAGGCTGGTGTAG  
AAAAGATCTTGTCTGCTCTGGAAATCCCGGACGTTGGTAATCTGTCTCAG  
GTAGTTGTAATGAAATCCAAGAACGACGAGGTATCACTAACAATGCA  
AAATGAATCTGCAGGACAACAATGGTAACGATATCGGTTTCATCGGTTT  
CCACCAGTTCAACAATATCGCTAAACTGGTTGCTTCCAAGTGTACAATC  
GTCAGATCGAACGTTCTCTCGCACTCTGGGTTGCTCTTGGGAGTTCATC  
CCGTTGATGACGGTTGGGGTGAACGTCCGCTGtaaGAATTC

B: BoNTA(H<sub>c</sub>) encoded protein (Version #1) SEQ ID NO: 2

MRLLSTFTEYIKNIINTSILNLRYESNHLIDLSRYASKINIGSKVNFDPIDKNQI  
QLFNLESSKIEVILKNAIVNSMYENFSTSFWRIPKYFNSISLNNEYTIINCME  
NNSGWKVSLNYGEIITLQDTQEIQRVVFKYSQMINISDYINRWIFVTITNN  
RLNNSKIYINGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHRYIWIWIKYFNLF  
DKELNEKEIKDLYDNQSNISGILKDFWGDYLYDKPYMLNLYDPNKEYVDV  
NNVGIRGYMYLKGPRGSVMTTNIYLNSSLYRGTKFIKKYASGNKDNIVRN  
NDRVYINVVVKNEYRLATNASQAGVEKILSALEIPDVGNLSQVVVMKSKN  
DQGITNKCKMNLQDNNNGNDIGFIGFHQFNIAKLVASNWNRYNIERSRTL  
GCSWEFIPVDDGWGERPL\*

FIGURE 2

**A: BoNTA(H<sub>c</sub>) synthetic gene (version #2) SEQ ID NO: 3**

GAATTCGAAACGatgTCTACCTTCACTGAATACATCAAGAACATCATCAAT  
ACCTCCATCCTGAACCTGCGCTACGAATCCAATCACCTGATCGACCTGTC  
TCGCTACGCTTCCAAAATCAACATCGGTTCTAAAGTTAACTTCGATCCGA  
TCGACAAGAATCAGATCCAGCTGTTCAATCTGGAATCTTCCAAAATCGA  
AGTTATCCTGAAGAATGCTATCGTATACAACCTCTATGTACGAAAACCTTCT  
CCACCTCCTTCTGGATCCGTATCCCGAAATACTTCAACTCCATCTCTCTG  
AACAATGAATACACCATCATCAACTGCATGGAAAACAATTCTGGTTGGA  
AAGTATCTCTGAACTACGGTGAAATCATCTGGACTCTGCAGGACACTCA  
GGAAATCAAACAGCGTGTTGTATTCAAATACTCTCAGATGATCAACATCT  
CTGACTACATCAATCGCTGGATCTTCGTTACCATCACCAACAATCGTCTG  
AATAACTCCAAAATCTACATCAACGGCCGTCTGATCGACCAGAAACCGA  
TCTCCAATCTGGGTAACATCCACGCTTCTAATAACATCATGTTCAAACCTG  
GACGGTTGTCGTGACACTACCGCTACATCTGGATCAAATACTTCAATCT  
GTTTCGACAAAGAACTGAACGAAAAAGAAATCAAAGACCTGTACGACAA  
CCAGTCCAATTCTGGTATCCTGAAAGACTTCTGGGGTGACTACCTGCAGT  
ACGACAAACCGTACTACATGCTGAATCTGTACGATCCGAACAAATACGT  
TGACGTCAACAATGTAGGTATCCGCGGTTACATGTACCTGAAAGGTCCG  
CGTGGTTCTGTTATGACTACCAACATCTACCTGAACTCTTCCCTGTACCG  
TGGTACCAAATTCATCATCAAGAAATACGCGTCTGGTAACAAGGACAAT  
ATCGTTCGCAACAATGATCGTGTATACATCAATGTTGTAGTTAAGAACAA  
AGAATACCGTCTGGCTACCAATGCTTCTCAGGCTGGTGTAGAAAAGATC  
TTGTCTGCTCTGGAAATCCCGGACGTTGGTAATCTGTCTCAGGTAGTTGT  
AATGAAATCCAAGAACGACCAGGGTATCACTAACAAATGCAAATGAAT  
CTGCAGGACAACAATGGTAACGATATCGGTTTCATCGGTTTCCACCAGTT  
CAACAATATCGCTAAACTGGTTGCTTCCAACCTGGTACAATCGTCAGATCG  
AACGTTCTCTCGCACTCTGGGTTGCTCTTGGGAGTTCATCCCGGTTGAT  
GACGGTTGGGGTGAACGTCCGCTGtaaGAATTC

**B: BoNTA(H<sub>c</sub>) encoded protein (Version #2) SEQ ID NO: 4**

MSTFTEYIKNIINTSILNLRYESNHLIDLSRYASKINIGSKVNFDPIDKNQIQLF  
NLESSKIEVILKNAIVYNSMYENFSTSFWIRIPKYFNSSISLNNEYTIINCMENNS  
GWKVSILNYGEIHWTLQDTQEIKQRVVFKYSQMINISDYINRWIFVTITNNRLN  
NSKIYINGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHRYIWIKYFNLFDKE  
LNEKEIKDLYDNQSNISGILKDFWGDYLYQYDKPYMLNLYDPNKYVDVNNV  
GIRGYMYLKGRGSVMTTNIYLNSSLYRGTKFIIKKYASGNKDNIVRNNDRV  
YINVVVKNKEYRLATNASQAGVEKILSALEIPDVGNLSQVVVMKSKNDQGI  
TNKCKMNLQDNNNGNDIGFIGFHQFNIAKLVASNWYNRQIERSSRTLGCSSW  
EFIPVDDGWGERPL\*

FIGURE 3

**A: BoNTA(H<sub>c</sub>) synthetic gene (Version #3) SEQ ID NO: 5**

GAATTCGAAACGatgGCCTCTACCTTCACTGAATACATCAAGAACATCATC  
AATACCTCCATCCTGAACCTGCGCTACGAATCCAATCACCTGATCGACCT  
GTCTCGCTACGCTTCCAAAATCAACATCGGTTCTAAAGTTAACTTCGATC  
CGATCGACAAGAATCAGATCCAGCTGTTCAATCTGGAATCTTCCAAAAT  
CGAAGTTATCCTGAAGAATGCTATCGTATACAACTCTATGTACGAAAAC  
TCTCCACCTCCTTCTGGATCCGTATCCCGAAATACTTCAACTCCATCTCTC  
TGAACAATGAATACACCATCATCAACTGCATGGAAAACAATTCTGGTTG  
GAAAGTATCTCTGAACTACGGTGAAATCATCTGGACTCTGCAGGACACT  
CAGGAAATCAAACAGCGTGTTGTATTCAAATACTCTCAGATGATCAACA  
TCTCTGACTACATCAATCGCTGGATCTTCGTTACCATCACCAACAATCGT  
CTGAATAACTCCAAAATCTACATCAACGGCCGTCTGATCGACCAGAAAC  
CGATCTCCAATCTGGGTAACATCCACGCTTCTAATAACATCATGTTCAAA  
CTGGACGGTTGTCGTGACACTCACCGCTACATCTGGATCAAATACTTCAA  
TCTGTTTCGACAAAGAAGTGAACGAAAAAGAAATCAAAGACCTGTACGAC  
AACCAGTCCAATTCTGGTATCCTGAAAGACTTCTGGGGTGACTACCTGCA  
GTACGACAAACCGTACTACATGCTGAATCTGTACGATCCGAACAAATAC  
GTTGACGTCAACAATGTAGGTATCCGCGGTTACATGTACCTGAAAGGTC  
CGCGTGGTTCTGTTATGACTACCAACATCTACCTGAACTCTTCCCTGTAC  
CGTGGTACCAAATTCATCATCAAGAAATACGCGTCTGGTAACAAGGACA  
ATATCGTTCGCAACAATGATCGTGTATACATCAATGTTGTAGTTAAGAAC  
AAAGAATACCGTCTGGCTACCAATGCTTCTCAGGCTGGTGTAGAAAAGA  
TCTTGTCTGCTCTGGAAATCCCGGACGTTGGTAATCTGTCTCAGGTAGTT  
GTAATGAAATCCAAGAACGACCAGGGTATCACTAACAAATGCAAAATGA  
ATCTGCAGGACAACAATGGTAACGATATCGGTTTCATCGGTTTCCACCAG  
TTCAACAATATCGCTAAACTGGTTGCTTCCAACCTGGTACAATCGTCAGAT  
CGAACGTTTCTCTCGCACTCTGGGTTGCTCTTGGGAGTTCATCCCGGTTG  
ATGACGGTTGGGGTGAACGTCCGCTGtaaGAATTC

**B: BoNTA(H<sub>c</sub>) encoded protein (Version #3) SEQ ID NO: 6**

MASTFTEYIKNIINTSILNLRYESNHLIDLSRYASKINIGSKVNFDPIDKNQIQL  
FNLESSKIEVILKNAIVYNSMYENFSTSWIRIPKYFNSISLNNEYTIINCMENN  
SGWKVSLNYGEIHWTLQDTQEIKQRVVFKEYSQMINISDYINRWIFVTITNNRL  
NNSKIYINGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHR YIWIKYFNLFDK  
ELNEKEIKDL YDNQSN SGILKDFWGDYLYDKPY YMLNLYDPNKYVDVNN  
VGIRGYMYLKGRGSVMTTNIYLNSSLYRGTKFIIKKYASGNKDNIVRNDR  
VYINVVVKNKEYRLATNASQAGVEKILSALEIPDVGNLSQVVVMKSKNDQ  
GITNKCKMNLQDNNGNDIGFIGFHQFNNAKLVASNWYNRQIERSSRTLGC  
SEFIPVDDGWGERPL\*

FIGURE 4

**A: BoNTB(H<sub>c</sub>) synthetic gene SEQ ID NO: 7**

GAATTCACGatgGCCAACAAATACAATTCCGAAATCCTGAACAATATCAT  
CCTGAACCTGCGTTACAAAGACAACAATCTGATCGATCTGTCTGGTTACG  
GTGCTAAAGTTGAAGTATACGACGGTGTTGAACTGAATGACAAGAACCA  
GTTCAAACCTGACCTCTTCCGCTAACTCTAAGATCCGTGTTACTCAGAATC  
AGAACATCATCTTCAACTCCGTATTCTGGACTTCTCTGTTTCCTTCTGGA  
TTCGTATCCCGAAATACAAGAACGACGGTATCCAGAATTACATCCACAA  
TGAATACACCATCATCAACTGCATGAAGAATAACTCTGGTTGGAAGATC  
TCCATCCGCGGTAACCGTATCATCTGGACTCTGATCGATATCAACGGTAA  
GACCAAATCTGTATTCTTCGAATACAACATCCGTGAAGACATCTCTGAAT  
ACATCAATCGCTGGTTCTTCGTTACCATCACCAATAACCTGAACAATGCT  
AAAATCTACATCAACGGTAAACTGGAATCTAATACCGACATCAAAGACA  
TCCGTGAAGTTATCGCTAACGGTGAAATCATCTTCAAACCTGGACGGTGA  
CATCGATCGTACCCAGTTCATCTGGATGAAATACTTCTCCATCTTCAACA  
CCGAACCTGTCTCAGTCCAATATCGAAGAACGGTACAAGATCCAGTCTTA  
CTCCGAATACCTGAAAGACTTCTGGGGTAATCCGCTGATGTACAACAAA  
GAATACTATATGTTCAATGCTGGTAACAAGAAGTCTTACATCAAACCTGA  
AGAAAGACTCTCCGGTTGGTGAAATCCTGACTCGTTCCAAATACAACCA  
GAACTCTAAATACATCAACTACCGCGACCTGTACATCGGTGAAAAGTTC  
ATCATCCGTCGCAAATCTAACTCTCAGTCCATCAATGATGACATCGTACG  
TAAAGAAGACTACATCTACCTGGACTTCTTCAACCTGAATCAGGAATGG  
CGTGTATACACCTACAAGTACTTCAAGAAAGAAGAAGAAAAGCTTTTCC  
TGGCTCCGATCTCTGATTCCGACGAACTCTACAACACCATCCAGATCAAA  
GAATACGACGAACAGCCGACCTACTCTTGCCAGCTGCTGTTCAAGAAAG  
ATGAAGAATCTACTGACGAAATCGGTCTGATCGGTATCCACCGTTTCTAC  
GAATCTGGTATCGTATTCTGAAGAATACAAGACTACTTCTGCATCTCCAA  
ATGGTACCTGAAGGAAGTTAAACGCAAACCGTACAACCTGAAACTGGGT  
TGCAATTGGCAGTTCATCCCGAAAGACGAAGGTTGGACCGAAtagtaaGAA  
TTC

**B: BoNTB(H<sub>c</sub>) encoded protein SEQ ID NO: 8**

MANKYNSEILNNIILNLRKYDNNLIDLSGYGAKVEVYDGVELNDKNQFKLT  
SSANSKIRVTQNQNIIFNSVFLDFSVSFWIRIPKYKNDGIQNYIHNEYTIINCM  
KNNSGWKISIRGNRIIWTLIDINGKTKSVFFEYNIREDISEYINRFFFVTITNNL  
NNAKIYINGKLESNTDIKDIREVIANGEIIFKLDGDIDRTQFIWMKYFSIFNTEL  
SQSNIEERYKIQSYSEYLKDFWGNPLMYNKEYYMFNAGNKNSYIKLKKDSP  
VGEILTRSKYNQNSKYINYRDLYIGEKFIIRKSNSSQSINDDIVRKEDIYIYLD  
FNLNQEWRYVYTYKYFKKEEEKLFLAPISDSDELYNTIQIKEYDEQPTYSCQL  
LFFKDEESTDEIGLIGHRFYYESGIVFEEYKDYFCISKWYLKEVKRKPYNLKL  
GCNWQFIPKDEGWTE\*\*

FIGURE 5

**A: BoNTC<sub>1</sub>(H<sub>c</sub>) synthetic gene SEQ ID NO: 9**

GAATTCACGatgACCATCCCATTCAACATCTTCTCCTACACCAACAACCTCC  
CTGTTGAAGGACATCATCAACGAGTACTTCAACAACATCAACGACTCCA  
AGATCCTGTCCCTGCAGAACCGTAAGAACACCTTGGTCGACACCTCCGG  
TTACAACGCCGAGGTCTCCGAGGAGGGTGACGTCCAGCTGAACCCAATC  
TTCCCATTGCGACTTCAAGCTGGGTTCCTCCGGTGAGGACAGAGGTAAGGT  
CATCGTCACCCAGAACGAGAACATCGTCTACAACCTCCATGTACGAGTCC  
TTCTCCATCTCCTTCTGGATCAGAATCAACAAGTGGGTCTCCAACCTTGCC  
AGGTTACACCATCATCGACTCCGTCAAGAACAACCTCCGGTTGGTCCATCG  
GTATCATCTCCAACCTTCTGGTCTTCACCCTGAAGCAGAACGAGGACTCC  
GAGCAGTCCATCAACTTCTCCTACGACATCTCCAACAACGCTCCTGGTTA  
CAACAAGTGGTTCTTCGTCACCGTCACCAACAACATGATGGGTAACATG  
AAGATCTACATCAACGGTAAGCTGATCGACACCATCAAGGTCAAGGAGT  
TGACCGGTATCAACTTCTCCAAGACCATCACCTTCGAGATCAACAAGATC  
CCAGACACCGGTCTGATCACCTCCGACTCCGACAACATCAACATGTGGA  
TCCGTGACTTCTACATCTTCGCCAAGGAGTTGGACGGTAAGGACATCAA  
CATCCTGTTCAACTCCTTGCAGTACACCAACGTCGTCAAGGACTACTGGG  
GTAACGACCTGAGATACAACAAGGAGTACTACATGGTCAACATCGACTA  
CTTGAACAGATACATGTACGCCAACTCCAGACAGATCGTCTTCAACACC  
AGACGTAACAACAACGACTTCAACGAGGGTTACAAGATCATCATCAAGC  
GTATCAGAGGTAACACCAACGACACCAGAGTCAGAGGTGGTGACATCCT  
GTACTTCGACATGACTATCAACAACAAGGCCTACAACCTGTTTCATGAAG  
AACGAGACCATGTACGCCGACAACCACTCCACCGAGGACATCTACGCCA  
TCGGTCTGCGTGAGCAGACCAAGGACATCAACGACAACATCATCTTCCA  
GATCCAGCCAATGAACAACACTTACTACTACGCTTCCCAGATCTTCAAGT  
CCAACCTCAACGGTGAGAACATCTCCGGTATCTGTTCCATCGGTACCTAC  
AGATTCCGTCTGGGTGGTGACTGGTACAGACACAACCTACTTGGTTCCAAC  
TGTCAGCAGGGTAACTACGCCTCCTTGCTGGAGTCCACTTCCACCCACT  
GGGGATTCTGTCCTCAGTCTCCGAGtaaatagGAATTC

**B: BoNTC<sub>1</sub>(H<sub>c</sub>) encoded protein SEQ ID NO: 10**

MTIPFNIFS YTNNSLLKDIINEYFNNINDSKILSLQNRKNTLVDTSGYNAEVSE  
EGDVQLNPFPDFKLGSSGEDRGKVIVTQENENIVYNSMYESFSISFWIRINK  
WVSNLPGYTIIDSVKNNSGWSIGIISNFLVFTLKQNEDEQSINFSDISNNAP  
GYNKWFFVTVTNNMMGNMKIYINGKLIDTIKVKELTGINFSKTITFEINKIPD  
TGLITSDSDNINMWIRDFYIFAKELDGKDINILFNSLQYTNVVKDYWGNDLR  
YNKEYYMVNIDYLNRYMYANSRQIVFNTRNNNDNFEGYKIIKRIRGNTN  
DTRVRGGDILYFDMTINNKAYNLFMKNETMYADNHSTEDIYAIGLREQTKD  
INDNIIIFIQPMNNTYYYASQIFKSNFNGENISGICSIGTYRFRLLGGDWYRHN  
YLVPTVKQGNYASLLESTSTHWGFVPVSE\*\*

FIGURE 6

**A: BoNTD(H<sub>c</sub>) synthetic gene SEQ ID NO: 11**

GAATTCACGatgCGTTTGAAGGCTAAGGTCAACGAGTCCTTCGAGAACAC  
CATGCCATTCAACATCTTCTCCTACACCAACAACCTCCTTGTTGAAGGACA  
TCATCAACGAGTACTTCAACTCCATCAACGACTCCAAGATCTTGTCCTTG  
CAGAACAAGAAGAACGCCTTGGTTCGACACCTCCGGTTACAACGCCGAGG  
TCAGAGTCGGTGACAACGTCCAGTTGAACACCATCTACACCAACGACTT  
CAAGTTGTCCTCTTCCGGTGACAAGATCATCGTCAACTTGAACAACAACA  
TCTTGTACTCCGCCATCTACGAGAACTCCTCTGTCTCCTTCTGGATCAAG  
ATCTCCAAGGACTTGACCAACTCCCACAACGAGTACACCATCATCAACT  
CCATCGAGCAGAACTCCGGTTGGAAGTTGTGTATCCGTAACGGTAACAT  
CGAGTGGATCTTGCAGGACGTCAACCGTAAGTACAAGTCCTTGATCTTCG  
ACTACTCCGAGTCCTTGTCCCACACCGGTTACACCAACAAGTGGTTCTTC  
GTCACCATCACCAACAACATCATGGGTTACATGAAGTTGTACATCAACG  
GTGAGTTGAAGCAGTCCCAGAAGATCGAGGACCTGGACGAGGTCAAGCT  
GGACAAGACCATCGTCTTCCGGTATCGACGAGAACATCGACGAGAACCAG  
ATGTTGTGGATCCGTGACTTCAACATCTTCTCCAAGGAGCTGTCCAACGA  
GGACATCAACATCGTCTACGAGGGTTCAGATCCTGAGGAACGTCATCAAG  
GACTACTGGGGTAACCCACTGAAGTTCGACACCGAGTACTACATCATCA  
ACGACAACATACATCGACCGTTACATCGCCCCAGAGTCCAACGTCCTGGT  
CCTGGTCCAGTACCCTGACCGTTCCAAGCTGTACACCGGTAACCCTATCA  
CCATCAAGTCCGTCTCCGACAAGAACCTTACTCCCGTATCCTGAACGGT  
GACAACATCATCCTGCACATGCTGTACAACCTCCCGTAAGTACATGATCAT  
CCGTGACACCGACACCATCTACGCCACCCAGGGTGGTGACTGTTCCAG  
AACTGTGTCTACGCCCTGAAGCTGCAGTCCAACCTGGGTAACCTACGGTAT  
CGGTATCTTCTCCATCAAGAACATCGTCTCCAAGAACAAGTACTGCTCCC  
AGATCTTCTCCTCCTTCCGTGAGAACACCATGCTGCTGGCCGACATCTAC  
AAGCCTTGGCGTTTCTCCTTCAAGAACGCCTACACTCCTGTGCGCGTCAC  
CAACTACGAGACCAAGCTGCTGTCCACCTCCTCCTTCTGGAAGTTCATCT  
CCCGTGACCCAGGTGGGGTCGAGtaatagGAATTC

**B: BoNTD(H<sub>c</sub>) encoded protein SEQ ID NO: 12**

MRLKAKVNESFENTMPFNIFS YTNNSLLKDIINEYFNSINDSKILSLQNKKNA  
LVDTSGYNAEVRVGDNVQLNTIYTNDFKLSSSGDKIIVNLNNNILYSAIYENS  
SVSFWIKISKDLTNSHNEYTIINSIEQNSGWKLCIRNGNIEWILQDVNRKYKS  
LIFDYSESLSHTGYTNKWFFVTITNNIMGYMKLYINGELKQSQKIEDLDEVK  
LDKTIVFGIDENIDENQMLWIRDFNIFSKELSNEDINIVYEGQILRNVIKDYW  
GNPLKFDTEYYIINDNYIDRYIAPESNVLVLVQYPDRSKLYTGNPITIKSVSD  
KNPYSRILNGDNILHMLYNSRKYMIIRDTDTIYATQGGDCSQNCVYALKLQ  
SNLGNYGIGIFSINKIVSKNKYCSQIFSSFRENTMLLADIYKPWRFSFKNAYTP  
VAVTNYETKLLSTSSFWKFI SRDPGWVE\*\*

FIGURE 7

**A: BoNTE(H<sub>2</sub>) synthetic gene SEQ ID NO: 13**

GAATTCACCatgGGAGAGAGTCAGCAAGAACTAAATTCTATGGTAACTGA  
TACCCTAAATAATAGTATTCCTTTTAAGCTTTCTTCTTATACAGATGATAA  
AATTTTAATTTCTACTTCAACAAGTTCTTCAAGAGAATTAAGTCTTCTTC  
CGTTTTAAACATGAGATACAAGAATGATAAATACGTCGACACTTCCGGT  
TACGACTCCAATATCAACATTAACGGTGACGTGTACAAGTACCCAACATA  
ACAAAAACCAATTCGGTATCTACAACGACAAGCTTACTGAGCTGAACAT  
CTCTCAAAACGACTACATTATCTACGACAACAAGTACAAGAAGTCTCTCTA  
TTTCTTTCTGGGTCAGGATTCCTAACTACGACAACAAGATCGTCAACGTT  
AACACGAGTACACTATCATCAACTGTATGAGAGACAACAAGTCCGGTT  
GGAAGGTCTCTCTTAACCACAACGAGATCATTTGGACCTTGCAAGACAA  
CGCAGGTATTAACCAAAAAGTTAGCATTCAACTACGGTAACGCAAACGGT  
ATTTCTGACTACATCAACAAGTGGATTTTCGTCACTATCACTAACGACAG  
ATTAGGTGACTCTAAGCTTTACATTAACGGTAACTTAATCGACCAAAAGT  
CCATTTTAACTTAGGTAACATTACGTTTCTGACAACATCTTATTCAAG  
ATCGTTAACTGCAGTTACACCAGATACATTGGCATTAGATACTTCAACAT  
TTTCGACAAGGAGTTAGACGAGACCGAGATTCAAACTTTATACAGCAAC  
GAACCTAACACCAATATTTTGAAGGACTTCTGGGGTAACTACTTGCTTTA  
CGACAAGGAATACTACTTATTAACGTTGTTAAAGCCAAACAAGTTCATT  
GATAGGAGAAAGGATTCTACTTTAAGCATTAAACAACATCAGAAGCACTA  
TTCTTTTAGCTAACAGATTATACTCTGGTATCAAGGTAAAGATCCAAAGA  
GTTAACAAGTCTTCTACTAACGATAACCTTGTTAGAAAGAACGATCAGGT  
CTATATTAAGTTCGTCGCTAGCAAGACTCACTTATTCCCATTATATGCTG  
ATACCGCTACCACCAACAAGGAGAAGACCATCAAGATCTCCTCCTCTGG  
CAACAGATTTAACCAAGTCGTCGTTATGAACTCCGTCGGTAACAAGTGT  
CCATGAACTTTAAAAATAATAATGGAAATAATATTGGGTTGTTAGGTTTC  
AAGGCAGATACTGTAGTTGCTAGTACTTGGTATTATACCCACATGAGAG  
ATCACACCAACAGCAATGGATGTTTTTGGAACTTTATTTCTGAAGAACAT  
GGATGGCAAGAAAAAataa

TagGGATCC GCGGCCGC ACGCGT CCCGGG ACTAGT GAATTC

**B: BoNTE(H<sub>2</sub>) encoded protein SEQ ID NO: 14**

MGESQQELNSMVTDTLNN SIPFKLSSYTDDKILISYFNKFFKRIKSSSVLNMR  
YKNDKYVDTSYGYSNININGDVYKYPTNKNQFGIYNDKLTENISQNDYIIY  
DNKYKNFSISFWVRIPNYDNKIVNVNNEYTIINC MRDNNSGWKVS LNHNH EII  
WTLQDNAGINQKLAFNYGNANGISDYINKWIFVTITNDRLGDSKLYINGNLI  
DQKSILNLGNIHVSDNILFKIVNCSYTRYIGIRYFNIFDKELDETEIQTLYSNEP  
NTNILKDFWGNLYLLYDKEYYLLNVLPNNFIDRRKDSTLSINNIRSTILLANR  
LYSGIKVKIQRVNNSSTNDNLVRKNDQVYIN FVASKTHLFLPLYADTATTNKE  
KTIKISSSGNRFNQVVMNSVGN NCTMNFKNNGNNGNIGLLGFKADTVVAST  
WYYTHMRDHTNSNGCFWNFISEEHGWQEK\*\*

**Agu 11**

AMINO ACID AND DESIGNED NUCLEOTIDE SEQUENCE

Asu II

TTC GAA ACG ATG ATT TTA ATT TCC TAC TTC AAC AAG TTC TTC AAG AGA ATT AAG TCT TCC GTT TTA AAC ATG AGA TAC AAG AAT GAT AAA TAC GTC

M I L I S Y F N K F F K R I K S S V L N M R Y K N D K Y V

GAC ACT TCC GGT TAC GAC TCC AAT ATC AAC ATT AAC CGT GAC GTG TAC AAG TAC CCA ACT AAC AAA AAC CAA TTC GGT ATC TAC AAC GAC AAG CTT ACT GAG CTG

D T S G Y D S N I N I N G D Y K Y K N F S I S F W V R I P N Y D N K I V N V

AAC ATC TCT CAA AAC GAC TAC ATT ATC TAC GAC AAC AAG TAC AAG AAC TTC TCT ATT TCT TTC TGG GTC AGA ATT CTT AAC TAC GAC AAC AAG ATC GTC AAC GGT

N I S Q N D Y I I Y D N K Y K N F S I S F W V R I P N Y D N K I V N V

AAC AAC GAG TAC ACT ATC AAC TGT ATG AGA GAC AAC AAC TCC GGT TGG AAG GTC TCT CTT AAC CAC AAC GAG ATC ATT TGG ACC TTG CAA GAC AAC GCA GGT

N N E Y T I I N C M R D N N S G W K V S L N H N E I I W T L Q D N A G

ATT AAC CAA AAG TTA GCA TTC AAC TAC GGT AAC GCA AAC GGT ATT TCT GAC TAC ATC AAC AAG TGG ATT TTC GTC ACT ATC ACT AAC GAC AGA TTA GGT GAC TCT

I N Q K L A F N Y G N A N G I S D Y I N K W I F V T I T N D R L G D S

AAG CTT TAC ATT AAC GGT AAC TTA ATC GAC CAA AAG TCC ATT TTA AAC TTA GGT AAC ATT CAC GTT TCT GAC AAC ATC TTA TTC AAG ATC GTT AAC TGC AGT TAC

K L Y I N G N L I D Q K S I L N L G N I H V S D N I L F K I V N C S Y

ACC AGA TAC ATT GGC ATT AGA TAC TTC AAC ATT TTC GAC AAG GAG TTA GAC GAG AOC GAG ATT CAA ACT TTA TAC AGC AAC GAA CCT AAC ACC AAT ATT TTG AAG

T R Y I G I R Y F N I F D K E L D E T E I Q T L Y S N E P N T N I L K

GAC TTC TGG GGT AAC TAC TTG CTT TAC GAC AAG GAA TAC TAC TTA AAC GTG TTA AAG CCA AAC AAC TTC ATT GAT AGG AGA AAG GAT TCT ACT TTA AGC ATT

D F W G N Y L L Y D K E Y Y L L N V L K P N N F I D R R K D S T L S I

AAC AAC ATC AGA ACG ACT ATT CTT TTA GCT AAC AGA TTA TAC TCT GGT ATC AAG GTT AAG ATC CAA AGA GTT AAG AAC TCT TCT ACT AAC GAT AAC CTT GTT AG

N N I R S T I L L A N R L Y S G I K V K I Q R V N N S S T N D N L V R

AAG AAC GAT CAG GTC TAT ATT AAC TTC GTC GGT AOC AAG ACT CAC TTA TTC CCA TTA TAT GCT GAT AOC GCT AOC AAC AAG GAG AAG AOC ATC AAC ATC TCC

K N D Q V Y I N F V A S K T H L F L P L Y A D T A T T N K E K T I K I S

TCC TCT GGC AAC AAG TTT AAC CAA GTC GTC GTT ATG AAC TCC GTC GGT AAC AAC TGT AOC ATG AAC TTT AAA AAT AAT AAT GGA AAT AAT ATT GGG TTG TTA GGT

S S G N R F N Q V V M N S V G N N C T M N F K N N G N N I G L L G

TTC AAG GCA GAT ACT GTA GTT GCT AGT ACT TGG TAT TAT AOC CAC ATG AGA GAT CAC AOC AAC AGC AAT GGA TGT TTT TGG AAC TTT ATT TCT GAA GAA CAT GGA

F K A D T V V A S T W Y T H M R D H T N S N G C F W N F I S E E H G

TGG CAA GAA AAA TAA TAG GGA TCC

W Q E K ter BamHI

$$\infty$$



FIGURE 9

**A: BoNTF(H<sub>c</sub>) synthetic gene SEQ ID NO: 15**

GAATTCACGatgTCCTACACCAACGACAAGATCCTGATCTTGTACTTCAAC  
AAGCTGTACAAGAAGATCAAGGACAACCTCCATCTTGGACATGAGATACG  
AAAACAATAAGTTCATCGACATCTCCGGTTACGGTTCCAACATCTCCATC  
AACGGTGACGTCTACATCTACTCCACCAATAGAAACCAGTTCGGAATCT  
ACTCCTCCAAGCCTTCCGAGGTCAACATCGCTCAGAACAAACGACATCAT  
CTACAACGGAAGATAACCAGAACTTCTCCATCTCCTTCTGGGTCCGTATCC  
CAAAGTACTTCAACAAGGTCAACCTGAATAACGAGTACACCATCATCGA  
CTGCATCCGTAACAATAACTCCGGATGGAAGATCTCCCTGAACTACAAC  
AAGATCATCTGGACCCTGCAGGACACCGCCGGTAACAATCAGAAGTTGG  
TCTTCAACTACACCCAGATGATCTCCATCTCCGACTACATCAACAAGTGG  
ATCTTCGTCACCATCACCAATAACCGTTTGGGAACTCCAGAATCTACAT  
CAACGGTAACTTGATCGACGAGAAGTCCATCTCCAACCTGGGTGACATC  
CACGTCTCCGACAACATTTTGTTCAGATCGTCGGTTGTAACGACACCCG  
TTACGTCGGGATCCGTTACTTCAAAGTCTTCGACACTGAGTTGGGTAAAG  
CCGAGATCGAGACCTTGTACTCCGACGAGCCTGACCCATCCATCCTGAA  
GGACTTCTGGGGTAACTACCTGCTGTACAACAAACGTTACTACTTGCTGA  
ACTTGTTGCGTACCGACAAGTCCATCACCCAGAACTCCAACCTTCTGAAC  
ATCAACCAGCAGAGAGGTGTCTACCAGAAGCCAAACATCTTCTCCAACA  
CCAGATTGTACACCGGAGTCGAGGTCATTATCAGAAAGAACGGATCTAC  
TGATATTTCCAACACCGATAACTTCGTCAGAAAGAACGATCTGGCTTACA  
TCAACGTTGTCGACAGAGATGTCGAATACCGTCTGTACGCCGATATCTCT  
ATCGCCAAACCTGAAAAGATCATCAAGCTGATCCGTACCTCTAACTCTA  
ACAACTCTCTGGGACAAATCATCGTCATGGACTCCATCGGTAATAACTGT  
ACCATGAACTTCCAGAACAAACACGGTGGAAACATCGGTTTGTGGGT  
TCCACTCCAACAACTTGGTCGCTTCCTCCTGGTACTACAACAACATCCGT  
AAGAACACCTCCTCCAACGGTTGCTTCTGGTCCTTCATCTCCAAGGAGCA  
CGGTTGGCAGGAGAACTaatagGAATTC

**B: BoNTF(H<sub>c</sub>) encoded protein SEQ ID NO: 16**

MSYTNDKILILYFNKLYKKIKDNSILDMRYENNKFIDISGYGSNISINGDVYIY  
STNRNQFGIYSSKPSEVNIAQNNDIYNGRYQNFSISFWVRIPKYFNKVNLLN  
EYTIIDCIRNNNSGWKISLNYNKIIWTLQDTAGNNQKLVFNYTQMISISDYIN  
KWIFVTITNNRLGNSRIYINGNLIDEKSISNLGDIHVSDNILFKIVGCNDTRYV  
GIRYFKVFDTELKTEIETLYSDEPDPSILKDFWGNLYLLYNKRYLLNLLRT  
DKSITQNSNFLNINQQRGVYQKPNIFSNTRLYTGVEVIIRKNGSTDISNTDNF  
VRKNDLAYINVVDRDVEYRLYADISIAKPEKIIKLRTSNSNNSLGQIIVMDSI  
GNNCTMNFQNNNGGNIGLLGFHSNNLVASSWYNNIRKNTSSNGCFWSFIS  
KEHGWQEN\*\*

FIGURE 10

**A: BoNTG(H<sub>c</sub>) synthetic gene SEQ ID NO: 17**

GAATTCACGatgAAGGACACCATCCTGATCCAGGTCTTCAACAACACTACATC  
TCCAACATCTCCTCCAACGCCATCCTGTCCCTGTCCTACCGTGGTGGTCG  
TCTGATCGACTCCTCCGGTTACGGAGCCACCATGAACGTCGGTTCGGACG  
TCATCTTCAACGACATCGGTAACGGTCAGTTCAAGCTGAACAACCTCCGA  
GAACTCCAACATCACCGCCCACCAGTCCAAGTTCGTCGTCTACGACTCCA  
TGTTTCGACAACCTTCTCCATCAACTTCTGGGTCCGTACCCCAAAGTACAAC  
AACAAACGACATCCAGACCTACCTGCAGAACGAGTACACCATCATCTCCT  
GTATCAAGAACGACTCCGGTTGGAAGGTCTCCATCAAGGGAAACCGTAT  
CATCTGGACCCTGATCGACGTCAACGCCAAGTCCAAGTCCATCTTCTTCG  
AGTACTCCATCAAGGACAACATCTCCGACTACATCAACAAGTGGTTCTCC  
ATCACCATCACCAACGACCGTCTGGGTAACGCCAACATCTACATCAACG  
GTTCCCTGAAGAAGTCCGAGAAGATCCTGAACCTGGACCGTATCAACTC  
CTCCAACGACATCGACTTCAAGCTGATCAACTGTACCGACACCACCAAG  
TTCGTCTGGATCAAGGACTTCAACATCTTCGGTCGTGAGCTGAACGCCAC  
CGAGGTCTCCTCCCTGTACTGGATCCAGTCCTCCACCAACACCCTGAAGG  
ACTTCTGGGGAAACCCACTGCGTTACGACACCCAGTACTACCTGTTCAAC  
CAGGGTATGCAGAACATCTACATCAAGTACTTCTCCAAGGCCTCCATGG  
GTGAGACCGCCCCTCGTACCAACTTCAACAACGCCGCCATCAACTACCA  
GAACCTGTACCTGGGTCTGCGTTTCATCATCAAGAAGGCCTCCAACCTCCC  
GTAACATCAACAACGACAACATCGTCCGTGAGGGTGACTACATCTACCT  
GAACATCGACAACATCTCCGACGAGTCCTACCGTGTCTACGTCCTGGTCA  
ACTCCAAGGAGATCCAGACCCAGCTGTTCCCTGGCCCCAATCAACGACGA  
CCCTACCTTCTACGACGTCTGTCAGATCAAGAAGTACTACGAGAAGACC  
ACCTACAACCTGTCAGATCCTGTGCGAGAAGGACACCAAGACCTTCGGAC  
TGTTCCGGTATCGGTAAGTTCGTCAAGGACTACGGTTACGTCTGGGACACC  
TACGACAACCTACTTCTGTATCTCCCAGTGGTACCTGCGTCGTATCTCCGA  
GAACATCAACAAGCTGCGTCTGGGATGTAACCTGGCAGTTCATCCCAGTC  
GACGAGGGTTGGACCGAGGtaatagGAATTC

**B: BoNTG(H<sub>c</sub>) encoded protein SEQ ID NO: 18**

MKDTILIQVFNNYISNISSNAILSLSYRGGRLIDSSGYGATMNVGSDVIFNDIG  
NGQFKLNSENSENITAHQSKFVVYDSMFDNFSINFWVRTPKYNNNDIQTYL  
QNEYTHISCIKND SGWKVSIKGNRIIWTIDVNAKSKSIFFEYSIKDNISDYINK  
WFSITITNDRLGNANIYINGSLKKSEKILNLDRLINSSNDIDFKLINCTDITKFKV  
WIKDFNIFGRELNATEVSSLYWIQSSTNTLKD F WGNPLRYDTQYYLFNQGM  
QNIYIKYFSKASMGETAPRTNFNNAAINYQNL YLGLRFIKKASNSRNINNDN  
IVREGDYIYLNIDNISDES YRVYVLVNSKEIQTQLFLAPINDDPTFYDVLQIKK  
YYEKT TYNCQILCEKDTKTFGLFGIGKFVKDYGYVWD TYDNYFCISQWYLR  
RISENINKLRLG CNWQFIPVDEGWTE\*\*

FIGURE 11

**A: BoNTA(H<sub>N</sub>) synthetic gene SEQ ID NO: 19**

atgGCTCTGAACGACCTGTGCATCAAAGTTAACAACCTGGGACCTGTTCTTC  
TCCCCGTCTGAAGACAACCTTCACTAACGACCTGAACAAAGGCGAAGAAA  
TCACCTCCGACACTAACATCGAAGCTGCTGAAGAAAACATCTCTCTGGA  
CCTGATCCAGCAGTACTACCTGACTTTCAACTTCGACAACGAACCGGAA  
AACATCTCCATCGAAAACCTGTCTTCCGACATCATCGGTCAGCTGGAAC  
GATGCCGAACATCGAACGCTTCCCGAACGGCAAGAAATACGAACACGGTA  
AAATACACCATGTTCCACTACCTGCGTGCTCAGGAATTTCGAACACGGTA  
AATCTCGTATCGCTCTGACTAACTCCGTTAACGAAGCTCTGCTGAACCCG  
TCTCGCGTTTACACCTTCTTCTCTTCCGACTACGTTAAGAAAGTTAACAA  
AGCTACTGAAGCTGCTATGTTCTGGGTTGGGTTGAACAGCTGGTTTACG  
ACTTCACCGACGAAACTTCTGAAGTTTCCACCACTGACAAAATCGCTGAC  
ATCACTATCATCATCCCGTACATCGGCCCGGCTCTGAACATCGGTAACAT  
GCTGTACAAAGACGACTTCGTTGGTGCTCTGATCTTCTCTGGCGCTGTTA  
TCCTGCTGGAATTCATCCCGGAAATCGCTATCCCGGTTCTGGGTACCTTC  
GCTCTGGTTTCTACATCGCTAACAAAGTTCTGACTGTTTCAGACCATCGA  
CAACGCTCTGTCTAAACGTAACGAAAAATGGGACGAAGTTTACAAATAC  
ATCGTTACTAACTGGCTGGCTAAAGTTAACACTCAGATCGACCTGATCCG  
TAAGAAGATGAAAGAAGCTCTGGAAAACCAGGCTGAAGCTACTAAAGC  
TATCATCAACTACCAGTACAACCAGTACACCGAAGAAGAAAAGAACAAC  
ATCAACTTCAACATCGATGACCTGTCTCTAACTGAACGAATCCATCAA  
CAAAGCTATGATCAACATCAACAAATTCCTGAACCAGTGCTCTGTTTCT  
ACCTGATGAACTCTATGATCCCGTACGGCGTTAAACGCCTGGAAGACTTC  
GACGCTTCCCTGAAAGACGCTCTGCTGAAATACATCCGTGACAACTACG  
GTACTCTGATCGGCCAGGTTGACCGTCTGAAAGACAAGGTTAACAAACAC  
CCTGTCTACTGACATCCCGTTCCAGCTGTCCAAATACGTTGACAACCAAGta  
a

**B: BoNTA(H<sub>N</sub>) encoded protein SEQ ID NO: 20**

MALNDLCIKVNNWDLFFSPSEDNFTNDLNKGEEITSDTNIEAAEENISLDLIQ  
QYYLTFNFDNEPENISIENLSSDIIGQLELMPNIERFPNGKKYELDKYTMFHY  
LRAQEFEGHKSRIALTNSVNEALLNPSRVYTFSSDYVKKVKNKATEAAMFL  
GWVEQLVYDFTDETSEVSTTDKIADITIIPYIGPALNIGNMLYKDDFVGALIF  
SGAVILLEFIPEIAPVLGTFALVSYIANKVLTQVQIDNALSQRNEKWDEVYK  
YIVTNWLAKVNTQIDLIRKKMKEALENQAEATKAIINYQYNQYTEEEKNNI  
NFNIDDLSSKLNESINKAMININKFLNQCSVSYLMNSMIPYGVKRLEDFFDASL  
KDALLKYIRDNYGTLIGQVDRCLKDKVNNLTSTDIPFQLSKYVDNQ\*

FIGURE 12

**A: BoNTB(H<sub>N</sub>) synthetic gene SEQ ID NO: 21**

atgGCTCCAGGAATCTGTATCGACGTCGACAACGAGGACTTGTTCTTCATC  
GCTGACAAGAACTCCTTCTCCGACGACTTGTCCAAGAACGAGAGAATCG  
AGTACAACACCCAGTCCAACCTACATCGAGAACGACTTCCCAATCAACGA  
GTTGATCTTGGACACCGACTTGATCTCCAAGATCGAGTTGCCATCCGAGA  
ACACCGAGTCCTTGACTGACTTCAACGTCGACGTCCCAGTCTACGAGAA  
GCAACCAGCTATCAAGAAGATTTTCACCGACGAGAACACCATCTTCCAA  
TACCTGTACTCTCAGACCTTCCCTTTGGACATCAGAGACATCTCCTTGAC  
CTCTTCCCTTCGACGACGCCCTGCTGTTCTCCAACAAGGTCTACTCCTTCTT  
CTCCATGGACTACATCAAGACTGCTAACAAGGTCGTCGAGGCCGGTTTG  
TTCGCTGGTTGGGTCAAGCAGATCGTCAACGATTTTCGTCATCGAGGCTAA  
CAAGTCCAACACCATGGACAAGATTGCCGACATCTCCTTGATTGTCCCAT  
ACATCGGTTTGGCCTTGAACGTCGGTAACGAGACCGCCAAGGGTAACTT  
CGAGAACGCTTTTCGAGATCGCTGGTGCCTCCATCTTGTTGGAGTTCATCC  
CAGAGTTGTTGATCCAGTCGTCGGTGCCTTCTTGTTGGAGTCCTACATC  
GACAACAAGAACAAGATCATCAAGACCATCGACAACGCTTTGACCAAGA  
GAAACGAGAAGTGGTCCGACATGTACGGTTTGATCGTCGCCCAATGGTT  
GTCCACCGTCAACACCCAATTCTACACCATCAAGGAGGGTATGTACAAG  
GCCTTGAACCTACCAGGCCCAAGCTTTGGAGGAGATCATCAAGTACAGAT  
ACAACATCTACTCCGAGAAGGAGAAGTCCAACATTAACATCGACTTCAA  
CGACATCAACTCCAAGCTGAACGAGGGTATTAACCAGGCCATCGACAAC  
ATCAACAACCTTCATCAACGGTTGTTCCGTCTCCTACTTGATGAAGAAGAT  
GATTCCATTGGCCGTCGAGAAGTTGTTGGACTTCGACAACACCCTGAAG  
AAGAACTTGTTGAACTACATCGACGAGAACAAGTTGTACTTGATCGGTT  
CCGCTGAGTACGAGAAGTCCAAGGTCAACAAGTACTTGAAGACCATCAT  
GCCATTCGACTTGTCCATCTACACCAACGACACCATCTTGATCGAGATGT  
TCtaa

**B: BoNTB(H<sub>N</sub>) encoded protein SEQ ID NO: 22**

MAPGICIDVDNEDLFFIADKNSFSDDLKSKNERIEYNTQSNIENDFPINELILD  
TDLISKIELPSENTESLTDNFNDVPVYEKQPAIKKIFTDENTIFQYLYSQTFPLD  
IRDISLTSSFDDALLFSNKVYSFFSMDYIKTANKVVEAGLFAGWVKQIVNDF  
VIEANKSNTMDKIADISLIVPYIGLALNVGNETAAGNFENAFEIAGASILLEFI  
PELLIPVVGAFLLSYIDNKNKIIKTIDNALTKRNEKWSDMYGLIVAQWLST  
VNTQFYTIKEGMYKALNYQAQALEEIIKYRYNIYSEKEKSNINIDFNDINSKL  
NEGINQAIDNINNFINCGSVSYLMKKMIPLAVEKLLDFDNTLLKKNLLNYIDE  
NKLYLIGSAEYEKSKVNKYLKTIMPFDLSIYTNDTILIEMF\*

FIGURE 13

**A: BoNTC<sub>1</sub>(H<sub>N</sub>) synthetic gene SEQ ID NO: 23**

atgTCCCTGTACAACAAGACCCTTGACTGTAGAGAGCTGCTGGTGAAGAA  
CACTGACCTGCCATTCATCGGTGACATCAGTGACGTGAAGACTGACATCT  
TCCTGCGTAAGGACATCAACGAGGAGACTGAGGTGATCTACTACCCAGA  
CAACGTGTGAGTAGACCAAGTGATCCTCAGTAAGAACACCTCCGAGCAT  
GGACAAGTAGACCTGCTCTACCCTAGTATCGACAGTGAGAGTGAGATCC  
TGCCAGGGGAGAATCAAGTCTTCTACGACAACCGTACCCAGAACGTGGA  
CTACCTGAACTCCTACTACTACCTAGAGTCTCAGAAGCTGAGTGACAAC  
GTGGAGGACTTCACTTTCACGCGTTCAATCGAGGAGGCTCTGGACAACA  
GTGCAAAGGTGTACACTTACTTCCCTACCCTGGCTAACAAGGTGAATGCC  
GGTGTGCAAGGTGGTCTGTTCCCTGATGTGGGCAAACGACGTGGTTGAGG  
ACTTCACTACCAACATCCTGCGTAAGGACACACTGGACAAGATCTCAGA  
TGTGTCAGCTATCATCCCCTACATCGGACCCGCACTGAACATCTCCAAC  
CTGTGCGTCGTGGAACTTCACTGAGGCATTTCGAGTCACTGGTGTCAAC  
ATCCTGCTGGAGGCATTCCCTGAGTTCACAATCCCTGCTCTGGGTGCATT  
CGTGATCTACAGTAAGGTCCAGGAGCGAAACGAGATCATCAAGACCATC  
GACAAGTGTCTGGAGCAGAGGATCAAGAGATGGAAGGACTCCTACGAGT  
GGATGATGGGAACGTGGTTGTCCAGGATCATCACCCAGTTCAACAACAT  
CTCCTACCAGATGTACGACTCCCTGAACTACCAGGCAGGTGCAATCAAG  
GCTAAGATCGACCTGGAGTACAAGAAGTACTCCGGAAGCGACAAGGAG  
AACATCAAGAGCCAGGTTGAGAACCTGAAGAACAGTCTGGACGTCAAG  
ATCTCGGAGGCAATGAACAACATCAACAAGTTCATCCGAGAGTGCTCCG  
TCACCTACCTGTTCAAGAACATGCTGCCTAAGGTCATCGACGAGCTGAA  
CGAGTTCGACCGAAACACCAAGGCAAAGCTGATCAACCTGATCGACTCC  
CATAACATCATCCTGGTCGGTGAGGTCGACAAGCTGAAGGCAAAGGTAA  
ACAACAGCTTCCAGAACTaa

**B: BoNTC<sub>1</sub>(H<sub>N</sub>) encoded protein SEQ ID NO: 24**

MSLYNKTLDCRELLVKNTDLPFIGDISDVKTDIFLRKDINEETEVIYYPDNVS  
VDQVILSKNTSEHGQLDLLYPSIDSESEILPGENQVFYDNRTQNVDYLN  
SY YLESQKLSDNVEDFTFTRSIEEALDNSAKVYTYFPTLANKVNAGVQGLFL  
MWANDVVEDFTTNILRKDTLDKISDVSAIIPYIGPALNISNSVRRGNFTEAFA  
VTGVTILLEAFPEFTIPALGAFVIYSKVQERNEIIKTIDNCLEQRIKRWKDSYE  
WMMGTWLSRIITQFNNISYQMYDSLNYQAGAIKAKIDLEYKKYSGSDKENI  
KSQVENLKNSLDVKISEAMNNINKFIRECSVTYLFKNMLPKVIDELNEFDRN  
TKAKLINLIDSHNILLVGEVDKLKAKVNNSFQN\*

FIGURE 14

**A: BoNTD(H<sub>N</sub>) synthetic gene SEQ ID NO: 25**

atggccAACTCCCGTGACGACTCCACCTGCATCAAGGTCAAGAACAACAGA  
CTGCCATACGTTGCCGACAAGGACTCCATCTCCCAGGAGATCTTCGAGA  
ACAAGATCATCACCGACGAGACCAACGTTCAAACTACTCCGACAAGTT  
CTCTTTGGACGAGTCCATCCTGGACGGTCAGGTCCCAATCAACCCAGAG  
ATCGTCGACCCACTGTTGCCAAACGTCAACATGGAGCCATTGAACTTGCC  
AGGTGAGGAGATCGTCTTCTACGACGACATCACCAAGTACGTCGACTAC  
TTGAACTCCTACTACTACTTGGAGTCTCAAAAGTTGTCTAACAACGTCGA  
GAACATCACCTTGACCACCTCCGTCGAGGAGGCCTTGGGTACTCTAACA  
AGATCTACACCTTCCTGCCATCCTTGGCTGAGAAGGTTAACAAGGGTGTT  
CAAGCTGGTTTGTTCCTGAACTGGGCCAACGAGGTCGTCGAGGACTTCA  
CCACCAACATCATGAAGAAGGACACCCTGGACAAGATCTCCGACGTCTC  
CGTCATCATCCCATACATCGGTCCAGCCTTGAACATCGGTAACCTCCGCCC  
TGAGAGGTAACCTCAACCAGGCCTTCGCCACCGCCGGTGTCGCCTTCCTG  
CTGGAGGGTTTCCCAGAGTTCACCATCCCAGCCCTGGGTGTCTTCACCTT  
CTACTCCTCCATCCAGGAGAGAGAGAAGATCATCAAGACCATCGAGAAC  
TGCTTGAGCAGAGAGTCAAGAGATGGAAGGACTCCTACCAGTGGATGG  
TTTCCAACCTGGCTGTCCAGAATCACCAACCAATTCAACCACATCAACTAC  
CAGATGTACGACTCCCTGTCCTACCAGGCCGACGCCATCAAGGCCAAGA  
TCGACCTGGAGTACAAGAAGTACTCCGGTTCGACAAGGAGAACATCAA  
GTCCCAGGTCGAGAACCTGAAGAACTCCTTGGACGTCAAGATCTCCGAG  
GCCATGAACAACATCAACAAGTTCATCCGTGAGTGTTCCGTACCTACCT  
GTTCAAGAACATGCTGCCAAAGGTCATCGACGAGCTGAACAAGTTCGAC  
CTGAGAACCAAGACCGAGCTGATCAACCTGATCGACTCCCACAACATCA  
TCCTGGTTGGTGAGGTTGACtaa

**B: BoNTD(H<sub>N</sub>) encoded protein SEQ ID NO: 26**

MANSRDDSTCIKVKNNRLPYVADKDSISQEIFENKIITDETNVQNYSDKFSLD  
ESILDGQVPINPEIVDPLLPNVNMEPLNLPGEIIVFYDDITKYVDYLNSYYL  
ESQKLSNNVENITLTSVEEALGYSNKIYTFLPSLAEEKVNKGVQAGLFLNWA  
NEVEDFTTNIMKKDTLDKISDVSVIPIYIPALNIGNSALRGNFNQAFATAG  
VAFLEGFPEFTIPALGVFTFYSSIQEREKIITIENTCLEQRVKRWKDSYQWM  
VSNWLSRITTQFNHINYQMYDSL SYQADAIKAKIDLEYKKYSGSDKENIKSQ  
VENLKNSLDVKISEAMNNINKFIRECSVTYLFKNMLPKVIDELNKFDLRTKT  
ELINLIDSHNIIIVGEVD\*

FIGURE 15

**A: BoNTE(H<sub>N</sub>) synthetic gene SEQ ID NO: 27**

atgTCCATCTGCATCGAGATCAACAACGGTGAGCTGTTCTTCGTGGCTTCC  
GAGAACAGTTACAACGATGACAACATCAACACTCCTAAGGAGATTGACG  
ACACCGTCACTTCTAACAACAACCTACGAAAACGACCTGGACCAGGTCAT  
CCTAAACTTCAACTCCGAGTCCGCCCTGGTCTGTCCGACGAGAAGCTGA  
ACCTGACCATCCAGAACGACGCTTACATCCCAAAGTACGACTCCAACGG  
TACATCCGATATCGAGCAGCATGACGTTAACGAGCTTAACGTCTTCTTCT  
ACTTAGACGCTCAGAAGGTGCCCGAGGGTGAGAACAACGTCAATCTCAC  
CTCTTCAATTGACACAGCCTTGTTGGAGCAGCCTAAGATCTACACCTTCT  
TCTCCTCCGAGTTCATCAACAACGTCAACAAGCCTGTGCAGGCCGCATTG  
TTCGTAAGCTGGATTTCAGCAGGTGTTAGTAGACTTCACTACTGAGGCTAA  
CCAGAAGTCCACTGTTGACAAGATCGCTGACATCTCCATCGTCGTCCCAT  
ACATCGGTCTGGCTCTGAACATCGGCAACGAGGCACAGAAGGGCAACTT  
CAAGGATGCCCTTGAGTTGTTGGGTGCCGGTATTTTGTGAGTTTCGAAC  
CCGAGCTGCTGATCCCTACCATCCTGGTCTTCACGATCAAGTCCTTCCTG  
GGTTCCTCCGACAACAAGAACAAGGTCATTAAGGCCATCAACAACGCCC  
TGAAGGAGCGTGACGAGAAGTGGAAGGAAGTCTATTCCTTCATCGTCTC  
GAACTGGATGACCAAGATCAACACCCAGTTCAACAAGCGAAAGGAGCA  
GATGTACCAGGCTCTGCAGAACCAGGTCAACGCCATCAAGACCATCATC  
GAGTCCAAGTACAACCTCCTACACCCTGGAGGAGAAGAACGAGCTTACCA  
ACAAGTACGATATCAAGCAGATCGAGAACGAGCTGAACCAGAAGGTCTC  
CATCGCCATGAACAACATCGACAGGTTCTGACCGAGTCCTCCATCTCCT  
ACCTGATGAAGCTCATCAACGAGGTCAAGATCAACAAGCTGCGAGAGTA  
CGACGAGAATGTCAAGACGTACCTGCTGAACTACATCATCCAGCACGGA  
TCCATCCTGtaa

**B: BoNTE(H<sub>N</sub>) encoded protein SEQ ID NO: 28**

MSICIEINNGELFFVASENSYNDDNINTPKEIDDTVTSNNNYENDLDQVILNF  
NSESAPGLSDEKLNLTIQNDA YIPKYDSNGTSDIEQHVDVNELNVFFYLDAQK  
VPEGENNVLNTSSIDTALLEQPKIYTFSSSEFINNVNKPVQAALFVSWIQQVL  
VDFTTEANQKSTVDKIADISIVVPYIGLALNIGNEAQKGNFKDALELLGAGIL  
LEFEPELLIPTILVFTIKSFLGSSDNKNKVIKAINNALKERDEKWKEVYSFIVS  
NWMTKINTQFNKRKEQMYQALQNQVNAIKTHIESKYNSYTL EEKNELTN KY  
DIKQIENELNQKVSIAMNNIDRFLTESSISYLMKLINEVKINKLREYDENVKT  
YLLNYIIQHGSIL\*

FIGURE 16

**A: BoNTF(H<sub>N</sub>) synthetic gene SEQ ID NO: 29**

atgGCCCCACCACGTCTGTGTATTAGAGTCAACAACCTCAGAATTATTCTTT  
GTCGCTTCCGAGTCAAGCTACAACGAGAACGATATTAACACACCTAAAG  
AGATTGACGATACTACCAACCTAAACAACAACCTACCGGAACAACCTGGA  
TGAGGTTATTTTGGATTACAACCTCACAGACCATCCCTCAAATTTCCAACC  
GTACCTTAAACACTCTTGTCCAAGACAACCTCCTACGTTCCAAGATACGAT  
TCTAACGGTACCTCAGAGATCGAGGAGTATGATGTTGTTGACTTTAACGT  
CTTTTTCTATTTGCATGCCCAGAAGGTGCCAGAAGGTGAAACCAACATCT  
CATTGACTTCTTCCATTGATACCGCCTTGTTGGAAGAGTCCAAGGATATC  
TTCTTTTCTTCGGAGTTTATCGATACTATCAACAAGCCTGTCAACGCCGC  
TCTGTTCAATTGATTGGATTAGCAAGGTCATCAGAGATTTTACCCTGAAG  
CTACTCAAAAGTCCACTGTTGATAAGATTGCTGACATCTCTTTGATTGTC  
CCCTATGTCGGTCTTGCTTTGAACATCATTATTGAGGCAGAAAAGGGTAA  
CTTTGAGGAGGCTTTTGAATTGTTGGGAGTTGGTATTTTGTGAGTTTG  
TTCCAGAACTTACCATTCTGTCATTTTAGTTTTTACGATCAAGTCCTACA  
TCGATTCATACGAGAACAAGAATAAAGCAATTAAAGCTATTAACAACCTC  
CTTGATCGAAAGAGAGGCTAAGTGGAAGGAAATCTACTCATGGATTGTA  
TCAAACCTGGCTTACTAGAATTAACACTCAATTTAACAAGAGAAAGGAGC  
AAATGTACCAGGCTCTGCAAAACCAAGTCGATGCTATCAAGACTGCAAT  
TGAATACAAGTACAACAACATACTTCCGATGAGAAGAACAGACTTGAA  
TCTGAATACAATATCAACAACATTGAAGAAGAGTTGAACAAGAAAGTTT  
CTTTGGCTATGAAGAATATCGAAAGATTTATGACCGAATCCTCTATCTCT  
TACTTGATGAAGTTGATCAATGAGGCCAAGGTTGGTAAGTTGAAGAAGT  
ACGATAACCACGTTAAGAGCGATCTGCTGAACTACATTCTCGACCACAG  
ATCAATCCTGGGAGAGCAGACAAACGAGCTGAGTGATTTGGTTACTTCC  
ACTTTGAACTCCTCCATTCCATTTGAGCTTTCTtaa

**B: BoNTF(H<sub>N</sub>) encoded protein SEQ ID NO: 30**

MAPPRLCIRVNNSEFFVASESSYNENDINTPKIEDDTNLNNNYRNNLDEVI  
LDYNSQTIPQISNRTLNTLVQDNSYVPRYDSNGTSEIEEYDVVDFNVFFYLH  
AQKVPEGETNISLTSSIDTALLEESKDIFFSSEFIDTINKPVNAALFIDWISKVIR  
DFTTEATQKSTVDKIADISLIVPYVGLALNIIIEAEKGNFEEAFELLGVGILLEF  
VPELTIPVILVFTIKSYIDSYENKNKAIKAINNSLIEREAKWKEIYSWIVSNWL  
TRINTQFNKRKEQMYQALQNQVDAIKTAIEYKYNNYTSDEKNRLESEYNIN  
NIEEELNKKVSLAMKNIERFMTESISYLMKLINEAKVGKLKKYDNHVKSDL  
LNYILDHRSILGEQTNELSDLVTSTLNSSIPFELS\*



FIGURE 17

**A: BoNTG(H<sub>N</sub>) synthetic gene SEQ ID NO: 31**

atggccAAAAATACCGGTAAATCTGAACAGTGTATTATTGTTAATAATGAG  
GATTTATTTTTTCATAGCTAATAAAGATAGTTTTTCAAAGATTTAGCTAA  
AGCAGAACTATAGCATATAATACACAAAATAACTATAGAAAATAAT  
TTTTCTATAGATCAGTTGATTTTAGATAATGATTTAAGCAGTGGCATAGA  
CTTACCAAATGAAAACACAGAACCATTTACAAATTTTGACGACATAGAT  
ATCCCTGTGTATATTAACAATCTGCTTTAAAAAAAATTTTTGTGGATGG  
AGATAGCCTTTTTGAATATTTACATGCTCAAACATTTCTTCTAATATAG  
AAAATCTACAATAACGAATTCATTAAATGATGCTTTAAGAAATAATAA  
TAAAGTCTATACTTTTTTTTCTACAAACCTTGTTGAAAAAGCTAATACAG  
TTGTAGGTGCTTCACTTTTTGTAACTGGGTAAAAGGAGTAATAGATGAT  
TTTACATCTGAATCCACACAAAAAAGTACTATAGATAAAGTTTCAGATGT  
ATCCATAATTATCCCTATATAGGACCTGCTTTGAATGTAGGAAATGAAA  
CAGCTAAAGAAAATTTTAAAAATGCTTTTGAAATAGGTGGAGCCGCTAT  
CTTAATGGAGTTTATTCCAGAAGTATTGTACCTATAGTTGGATTTTTTAC  
ATTAGAATCATATGTAGGAAATAAAGGGCATATTATTATGACGATATCC  
AATGCTTTAAAGAAAAGGGATCAAAAATGGACAGATATGTATGGTTTGA  
TAGTATCGCAGTGGCTCTCAACGGTTAATACTCAATTTTATACAATAAAA  
GAAAGAATGTACAATGCTTTAAATAATCAATCACAAGCAATAGAAAAAA  
TAATAGAAGATCAATATAATAGATATAGTGAAGAAGATAAAATGAATAT  
TAACATTGATTTTAATGATATAGATTTTAAACTTAATCAAAGTATAAATT  
TAGCAATAACAATATAGATGATTTTATAAACCAATGTTCTATATCATAT  
CTAATGAATAGAATGATTCCATTAGCTGTAAAAAAGTTAAAAGACTTTG  
ATGATAATCTTAAGAGAGATTTATTGGAGTATATAGATACAAATGAACT  
ATATTTACTTGATGAAGTAAATATTCTAAAATCAAAGTAAATAGACAC  
CTAAAAGACAGTATACCATTTGATCTTTCCTACTATATACCtaa

**B: BoNTG(H<sub>N</sub>) encoded protein SEQ ID NO: 32**

MAKNTGKSEQCIIVNNEDLFFIANKDSFSKDLAKAETIAYNTQNNTIENNFSI  
DQLILDNDLSSGIDLPNENTEPFTNFDDIDIPVYIKQSALKKIFVDGDSLFEYL  
HAQTFPSNIENLQLTNSLNDALRNNNKVYTFSTNLVEKANTVVGASLFVN  
WVKGVIDDFTSESTQKSTIDKVSDVSIIPYIGPALNVGNETAKENFKNAFEIG  
GAAILMEFIPELIVPIVGFFTLESYVGNKGHIIMTISNALKKRDQKWTDMYGL  
IVSQWLSTVNTQFYTIKERMYNALNNQSQAIEKIIDQYNRYSEEDKMNINI  
DFNDIDFKLNQSINLAINNIDDFINQCSISYLMNRMIPLAVKKLKDFDDNLKR  
DLLEYIDTNELYLLDEVNILKSKVNRHLKDSIPFDLSLYT\*

FIGURE 18

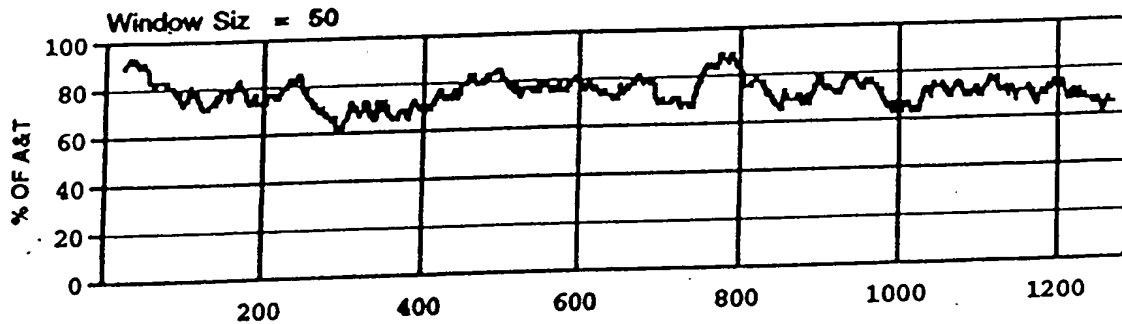
**A: First BoNTF(Hc) gene: SEQ ID NO: 33**

GAATTCACGatgTCTTACACTAACGACAAAATCCTGATCCTGTACTTCAAC  
AAACTGTACAAAAAATCAAAGACAACCTCTATCCTGGACATGCGTTACG  
AAAACAACAAATTCATCGACATCTCTGGCTATGGTTCTAACATCTCTATC  
AACGGTGACGTCTACATCTACTCTACTAACCGCAACCAGTTCGGTATCTA  
CTCTTCTAAACCGTCTGAAGTAAACATCGCTCAGAACAACGACATCATCT  
ACAACGGTCGTTACCAGAACTTCTCTATCTCTTTCTGGGTTTCGTATCCCG  
AAATACTTCAACAAAGTTAACCTGAACAACGAATACACTATCATCGACT  
GCATCCGTAACAACAACCTCTGGTTGGAAAATCTCTCTGAACTACAACAA  
AATCATCTGGACTCTGCAGGACACTGCTGGTAACAACCAGAACTGGTT  
TTCAACTACACTCAGATGATCTCTATCTCTGACTACATTAATAAATGGAT  
CTTCGTTACTATCACTAACAACCGTCTGGGTAACCTCTCGTATCTACATCA  
ACGGTAACCTGATCGATGAAAAATCTATCTCTAACCTGGGTGACATCCA  
CGTTTCTGACAACATCCTGTTCAAATCGTTGGTTGCAACGACACGCGTT  
ACGTTGGTATCCGTTACTTCAAAGTTTTTCGACACTGAACTGGGTAAAAC  
GAAATCGAACTCTGTACTCTGACGAACCGGACCCGTCTATCCTGAAAG  
ACTTCTGGGGTAACTACCTGCTGTACAACAAACGTTACTACCTGCTGAAC  
CTGCTCCGGACTGACAAATCTATCACTCAGAACTCTAACTTCCTGAACAT  
CAACCAGCAGCGTGGTGTATTATCAGAAACCTAATATCTTCTCTAACACTC  
GTCTGTACACTGGTGTGGAAGTTATCATCCGTAAAAACGGTTCTACTGAC  
ATCTCTAACACTGACAACTTCGTACGTAAAAACGACCTGGCTTACATCAA  
CGTTGTTGACCGTGACGTTGAATACCGTCTGTACGCTGACATCTCTATCG  
CTAAACCGGAAAAAATCATCAAACTGATCCGTACTTCTAACTCTAACAA  
CTCTCTGGGTCAGATCATCGTTATGGACTCGATCGGTAACAACCTGCACTA  
TGAACCTCCAGAACAACAACGGTGGTAACATCGGTCTGCTGGGTTTCCA  
CTCTAACAACTGGTTGCTTCTTCATGGTACTACAACAACATCCGTAAAA  
ACACTTCTTCTAACGGTTGCTTCTGGTCTTTCATCTCTAAAGAACACGGTT  
GGCAGGAAAACtaaGAATTC

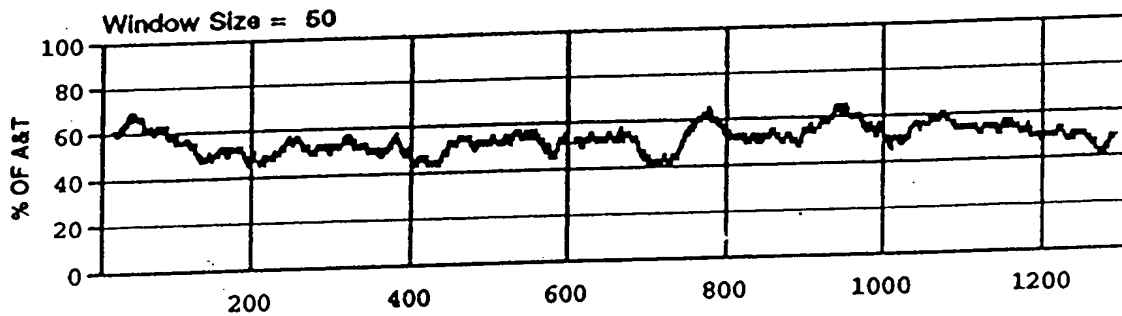
**B: BoNTF(Hc) #1 encoded protein: SEQ ID NO: 34**

MSYTNDKILILYFNKLYKKIKDNSILDMRYENNKFIDISGYGSNISINGDVYIY  
STNRNQFGIYSSKPSEVNIAQNNDIIYNGRYQNFSISFWVRIPKYFNKVNLLN  
EYTIIDCIRNNNSGWKISLNYNKIIWTLQDTAGNNQKLVFNQTQMISISDYIN  
KWIFVTITNNRLGNSRIYINGNLIDEKSISNLGDIHVSDNILFKIVGCNDTRYV  
GIRYFKVFDTELKTEIETLYSDEPDPSILKDFWGNLYLLYNKRYYLLNLLRT  
DKSITQNSNFLNINQQRGVYQKPNIFSNTRLYTGVEVIIRKNGSTDISNTDNF  
VRKNDLAYINVVDRDVEYRLYADISIAKPEKIIKLIRTSNSNNSLGQIIIVMDSI  
GNNCTMNFQNNNGNIGLLGFHSNNLVASSWYYNNIRKNTSSNGCFWSFIS  
KEHGWQEN\*

### A: Natural BoNTF(Hc) Gene



### B: First BoNTF(Hc) Synthetic Gene



### C: Second BoNTF(Hc) Synthetic Gene

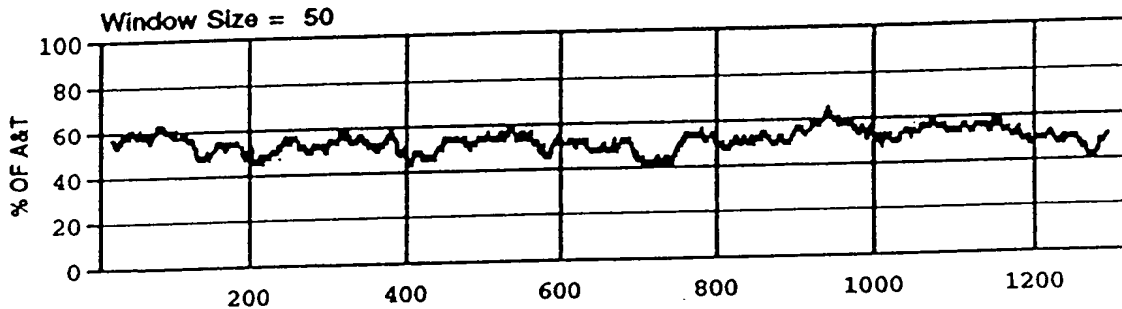
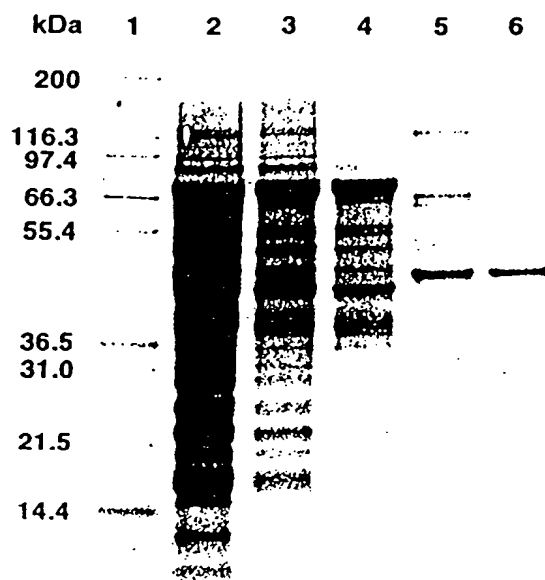


Fig 19

A



B

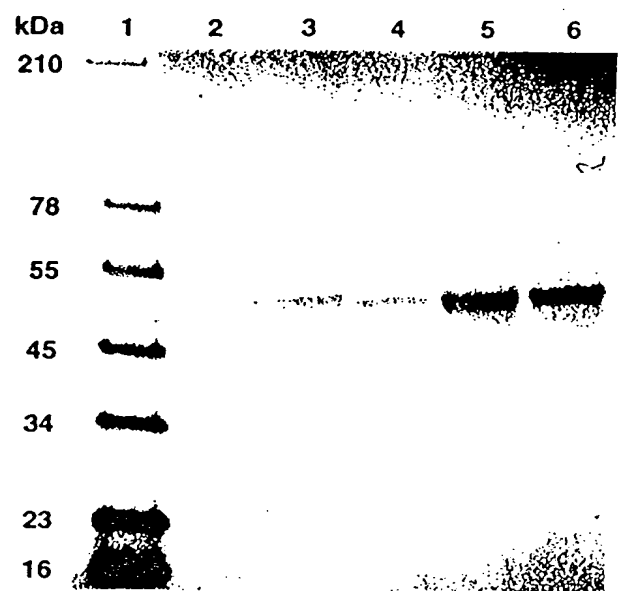


Fig 20

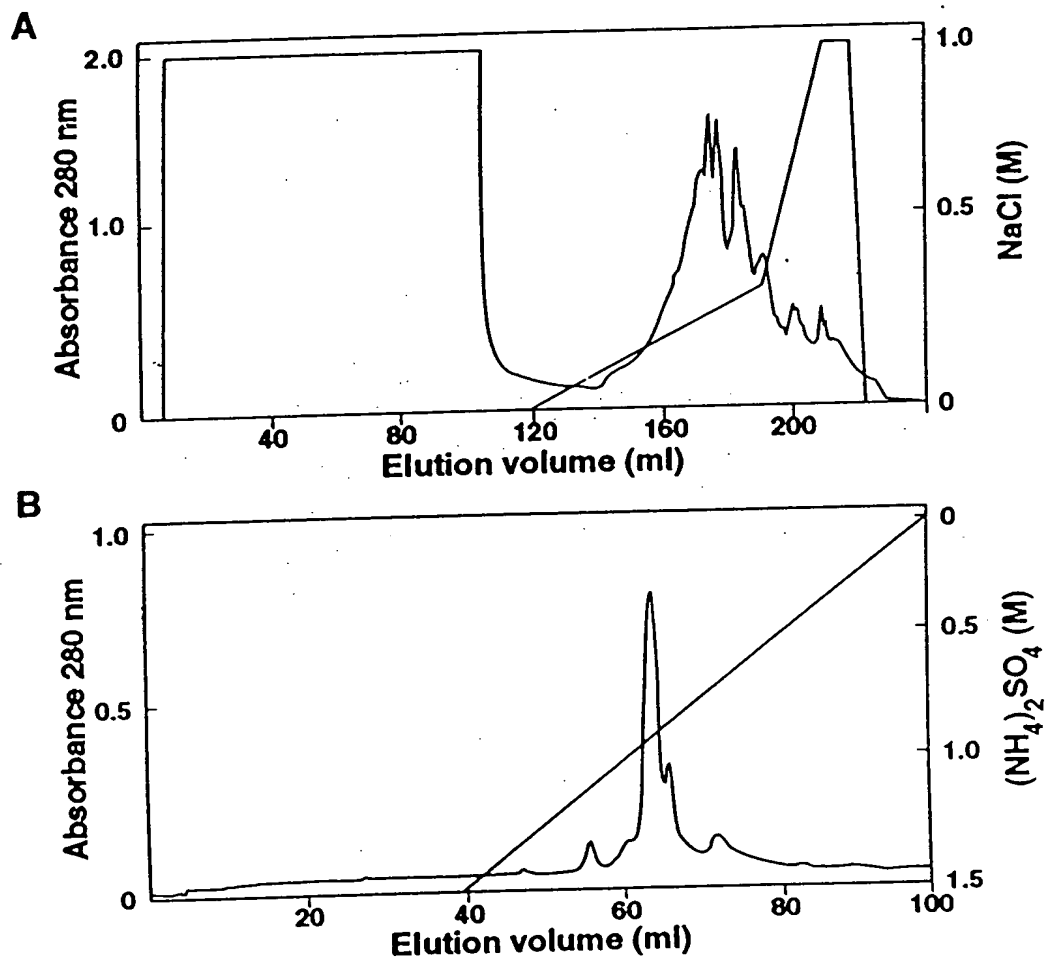


Fig 21

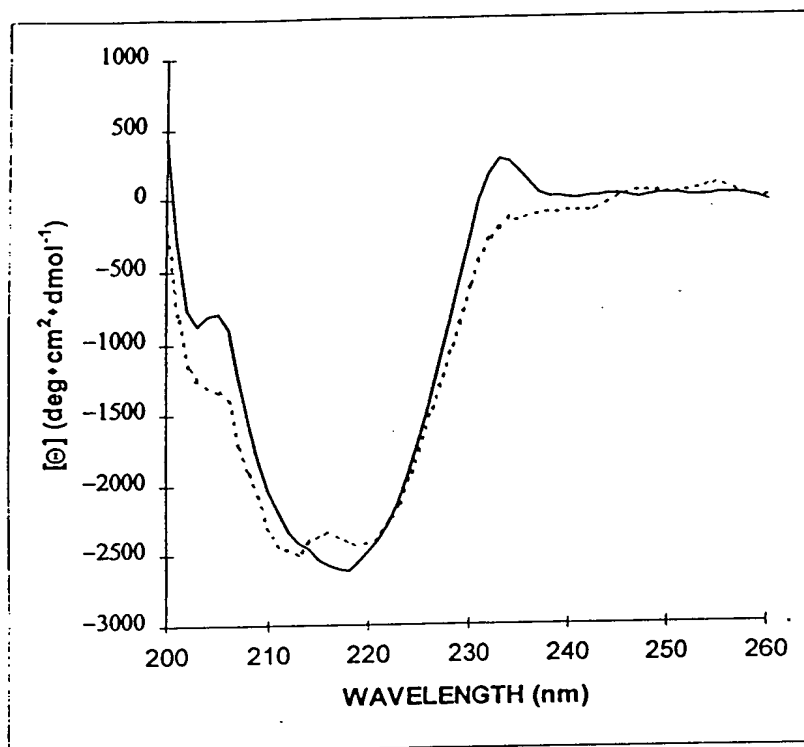


Fig 22